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Dehydrothiotoluidin: Its Isomers, Homologues, Analogues, and Derivatives.

DISSERTATION

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY

BY

MARTIN MEYER, B.S., M.A.

NEW YORK CITY

1921

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ACKNOWLEDGMENT AND DEDICATION

To Professor Marston Taylor Bogert to whose inspiration, suggestion, and constant interest, such merit as this work may possess is due.

M. M.

ORGANIC RESEARCH LABORATORIES,
HAVEMEYER HALL, COLUMBIA UNIVERSITY,
MAY, 1921

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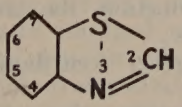
Dehydrothiotoluidin: Its Isomers, Homologues, Analogues, and Derivatives.

Introduction and Purpose

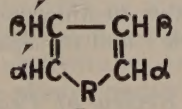
The chemistry of the organic sulphur compounds is one of the widest and most interesting divisions of the broad and attractive extent of the science, and in variety of properties, multiplicity of applications, and novelty of the reactions involved, is at least equal to, and certainly is excelled by no other. No matter what we choose as the criterion of our judgment we can meet all of the requirements without passing the boundaries of this field, be it medicinals, perfumes, dyes, explosives, or plastics, there is hardly a reaction that does not find its analogue, and in addition there are many here that can not be duplicated elsewhere.

In the chemistry of the dyestuffs, however, the sulphur compounds are pre-eminent. Of all the glorious colors which the chemist has contributed to mankind in his efforts to duplicate the iridescent beauty of the rainbow, the most beautiful and permanent are found in this group, the sulphides, the thioindigos, the thiazines, the thiazoles, and many others, the mere enumeration of which with their classes and sub-classes would fill a volume.

Among the most interesting of all from both academic and commercial standpoints are the five-membered nitrogen and sulphur heterocycles, more particularly the six-five bicyclic ones, or benzothiazoles. Of these the simplest is benzothiazole, or methenyl base as it is termed by Hofmann, to which the indicated structure is assigned. It may be observed that two



arrangements of the atoms in the smaller ring are possible. The nomenclature of the typical five-membered heterocycle is given by Richter as follows:



and in this system all of the compounds mentioned herein are substituted beta-thiazoles, the principal substitution being the in-

corporation of the alpha-beta carbon atoms into a second benzol nucleus. The compound shown above is then benzo-beta-thiazole, and it is further suggested that for the sake of simplicity in nomenclature the positions in this be numbered as shown, which is also more in uniformity with the system appled to the thiazines and other heterocyclic compounds. This will be followed throughout this paper.

The homologues and derivatives of the compound just given offer a peculiarly attractive field for research, because of the variety of their properties and their commercial importance. To substantiate this statement without, at this point, going into too much detail, a few examples may be cited. By the fusion of benzanilide with sulphur, A. W. Hofmann prepared what he called benzenylortho-aminothiophenol, which in the system just recommended, is 2-phenyl-benzothiazole. The compound, wholly unlike any other known substance of its type, has a pleasant, highly aromatic odor, somewhat suggestive of tea-roses or geraniums, which led its discoverer to term it also "Rosenkörper." Some of the derivatives of this series are dyes. A. H. Green, on fusing paratoluidin with sulphur, found primulin and dehydrothiotoluidin, which are well known because of their practical value, since the annual production of direct cotton dyes exceeds all others, being closely rivalled only by acid wool colors, and all the dyes of this group are direct cotton colors.

The last-named two substances are formed simultaneously in the same reaction, and it is an odd coincidence that while immediately after the original work, the former was the important product, today the latter is the more valuable. Nevertheless, in recent years comparatively little work has been done, or at any event, has been published, with them, and up to the present no entirely satisfactory method has been developed for preparing dehydrothiotoluidin in a state of purity, and the discovery of one would probably make it an even more important intermediate than it is. Further study of the reaction by which it is formed is therefore highly desirable.

With this brief introduction, the objects of this dissertation may be stated as follows:

1. To make some further contributions to the chemistry of the benzothiazole group.
2. To derive a relation between the thiazole structure and tinctorial value.
3. To determine the relation between the thiazole structure and odor.
4. To prepare pure dehydrothiotoluidin (6 methyl 2 para-aminophenyl benzothiazole) and to separate it from the primulin simultaneously formed.

Historical Review of Previous Work

Although the volume of research which has been accomplished in this field is quite large, and the compounds important, most

textbooks omit it entirely or dismiss it with a few lines, and even the original papers do not give much information about other work. No really acceptable summary of all of the work has ever been published, and, as it would be very useful to new investigations in the group, it is this which has led to the rather complete form in which the history is presented. Furthermore, the second and third objects of this investigation make a knowledge of what compounds have been prepared, and of their properties essential, and these are given at the end.

The credit for the discovery of, and original work upon the compounds of this group belongs to August Wilhelm von Hofmann (born April 8, 1818, died May 5, 1892), one of Liebig's illustrious pupils, and without whose work organic chemistry, as we know it today, would indeed be much the poorer. As his biographers, Jacob Volhard and Emil Fischer, whose pre-eminence in chemistry needs no further eulogy, say:[1]

"Out of the great number of chemists who, come forth from Liebig's school in the second half of the last century, have made themselves useful as teachers and investigators in the broadening and advancing of our knowledge, August Wilhelm von Hofmann towers above all others in the number and importance of his discoveries, in the success of his teaching, in the fruitfulness of his influence on the chemical industry, and in the range of his directing influence as an author." Not the least among these were his researches upon the benzothiazoles.

In 1874, Sell and Zierold[2] succeeded in preparing isocyanphenyl-chloride from phenyl mustard oil by the direct action of chlorine. A few years later Hofmann[3] conceived the idea of making the same substance from the mustard oil using PCl_5, expecting that the reaction would take place in this manner:

$$C_7H_5NS + PCl_5 = C_7H_5NCl_2 + PCl_3S$$

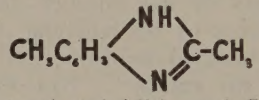
Upon actually performing the experiment he found that while some of the substance was indeed changed in this way, distillation of the reaction products yielded a portion boiling at 248° C. that contained a chlorinated mustard oil of a totally different type. The new substance was an oil of aromatic odor, B.P. 248° C., soluble in alcohol, from which it was precipitated by water, and upon a complete elementary analysis as a basis he assigned the empirical formula C_7H_4NSCl to it. It did not resemble in the least the compound for which he had been looking, and he proceeded to investigate its reactions. By acid hydrolysis he obtained $C_7H_4NS(OH)$ as a white solid (M.P. 136°, Jacobson later 139°), which exhibited phenolic properties, so he assumed the presence of an hydroxyl group. Dünner[4] had previously prepared hydroxy-phenyl mustard oil which did not resemble this compound. The action of ammonia on the compound yielded the amine as an oil of aromatic odor, while aniline gave the anilide, a white, odorless solid (M.P. 159°). Although at

this time he really did no work upon the structure of these substances, they were the first of the benzothiazoles, for as he showed later, they are all 2-substituted derivatives.

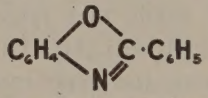
During the same year[5] Hofmann became interested in a different type of sulphur compound. Merz and Weith[6] had, by the action of sulphur on aniline, obtained a thioaniline which later proved to be identical with that prepared by Krafft[7] who demonstrated that it was a phenyl sulphide. It occurred to Hofmann that if, instead of employing aniline, he used benzanilide, or as he called it, phenyl-benzamide, in place of $NH_2C_6H_4—S—C_6H_4NH_2$, he should obtain a benzoylated thioaniline. On actually performing the experiment he found a reaction quite different from his expectations, and prepared in this way a substance which crystallized from alcohol in colorless needles (M.P. 115° C.) and had a pleasant, fragrant odor, resembling tea-roses or geraniums. Analysis indicated the empirical formula $C_{13}H_9NS$, and he showed the reaction by which it was formed to be:

$$C_{13}H_{11}NO + S = C_{13}H_9NS + H_2O$$

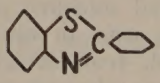
Hobrecker[8] earlier had synthesized a compound to which he assigned the formula

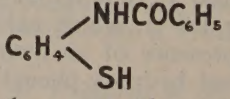


by reducing nitro-acetorthotoluidid, and Ladenburg,[9] and later Wund,[10] had prepared similar bases by the condensation of diamines with acids, and finally, studying the condensation of ortho-aminophenols with acids, Ladenburg[11] had made a substance which he wrote



The analogy to his own case was immediately apparent, and Hofmann assigned the formula



to the "Rosenkörper." To establish this fact more definitely, he then proceeded to show that, as would be expected from its structure, it yields, on hydrolysis, orthoamino-thiophenol and benzoic acid, and that it could be prepared from these two by the formation of an intermediate 

This was the first compound of the group whose structure could in any sense be said to have been proved. He now went back to his original chlorphenyl mustard oil and repeated his work,

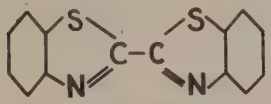
adding some more, and preparing a number of new compounds listed at the end of the section.

Then realizing that his previous article contained no proof of the structure of the chlor mustard oil, he proceeded to investigate its reactions still further. By reduction with tin in concentrated hydrochloric acid, he obtained C_7H_5NS, a liquid, heavier than water and insoluble in it, soluble in ethyl alcohol and carbon disulphide, having a burning taste, and a characteristic odor resembling somewhat that of the pyridines and the plant bases. It is isomeric with the mustard oils and thiocyanates and forms an addition product with methyl iodide which is soluble in water from which it crystallizes in colorless needles, M.P. 210°. The new base reacted with benzoyl chloride—

$$C_7H_5NS + C_7H_5OCl = C_{13}H_9NS + CO + HCl$$

This compound proved to be identical with that which he had previously obtained by the fusion of benzanilide with sulphur, and established beyond reasonable doubt, the structure of the new substances, which he then named on this basis. By this method he contributed further new compounds listed at the end.

Up to this time the only general method by which the benzothioazoles could be prepared, which was recognized as such, was that by which the just mentioned ones were prepared, that is, the condensation of ortho-aminothiophenols and acids, acid anhydrides, chlorides, and amides, but also in 1880[12] he conceived the idea that the reaction by which "Rosenkörper" had been synthesized might be applied with appropriate changes to the synthesis of homologues. Immediately he proceeded to investigate the behaviour of anilides on fusion with sulphur, obtaining from formanilide a small amount of methenyl base or benzothiazole, from acetanilide slight quantities of ethenyl base, or 2-methyl benzothiazole, but much larger yields of a new substance which had the empiric formula $C_{14}H_8N_2S_2$, and to which he assigned on the basis of several syntheses the structure:



oxalaminothiophenol (2:bis-benzothiazole [M.P. 306]). It crystallizes from alcohol in white needles although the solubility is very slight. No good proof of its structure was given, however, for several years.

Following this he prepared a number of the homologues of this compound, using the dibasic aliphatic acids and ortho-aminothiophenol. Only a year later Hess,[13] after having prepared the aminothiocresols, became interested in this general reaction, and using 3 sulphydroxy 4 amino toluene contributed several new compounds which will be given later.

Interest in these new sulphur compounds now became quite general. Two years after the work just described, Tiemann

and Piest[14] succeeded in preparing the "Rosenkörper" by a new method, the fusion of phenylanilino acetic nitrile which they happened to be studying, with sulphur. They demonstrated that the reaction proceeded according to the equation:

$$C_6H_5CH(C_6H_5NH)CN + 2S = C_{13}H_9NS + H_2S + HCN$$

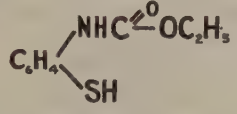
and identified the product by its melting point and ultimate analysis.

Then in 1886 P. Jacobson[15] published the first of a series of important contributions to the chemistry of the benzothiazoles. Thiobenzaldehyde had already been prepared by Klinger[16] and from this thiobenzanilide, which was also prepared by Leo[17] (and later by Gatterman—vide experimental part), by heating with aniline, but in repeating this work and studying the products of the reaction (stilbene and thiobenzanilide) Jacobson found also some of Hofmann's "Rosenkörper." The only explanation that he could give for its formation was that of oxidation of the thiobenzanilide, and to test the validity of his reasoning he oxidized a portion in alkaline solution with potassium ferricyanide and showed that about 60% of the product was the expected phenyl-benzothiazole. A new method of synthesis had been developed, for he recognized at once the generalization that could be drawn from this experiment, and proceeded to prepare the 2 methyl-benzothiazole, and claimed to have obtained benzothiazole itself, by the oxidation of the corresponding thioanilides, though in the case of the last mentioned, he was later disputed by Hofmann.

Apropos of the thioanilides a rather curious coincidence may be mentioned. Leo, in a disssertation for his doctor's degree at Bonn, 1878, under the title of thioanilides, described a substance which he prepared by the distillation of thiobenzanilid in the presence of air, and to which he assigned the formula $C_{27}H_{20}N_2S_2$. From his observations of the properties of the substance it was evidently the "Rosenkörper," and if his analytical work had been a little more accurate, and he had been able to appreciate the significance of his discovery, the credit for the original work in this field would have gone to him, for his work appeared several months before Hofmann's first paper.

In 1887[18] Hofmann published some further work on the chemistry of this series. He treated ortho-aminothiophenol with carbon disulphide expecting to find a derivative of thiocarbanilid, but obtained instead a body whose empiric formula was $C_7H_5NS_2$ and which he showed readily was 2-sulphhydrobenzothiazole and could be prepared from chlorbenzothiazole and sodium sulphydrate. By oxidation of this compound he made a 2:2 benzothiazole disulphide, shining, silvery plates from benzol, M.P. 180° (Jacobson later 186°) and by methylation the thioether, colorless prisms from dilute ethyl alcohol, M.P. 52°. The latter had an odor resembling that of benzothiazole itself, and also was quite similar to the ethoxy derivative already made.

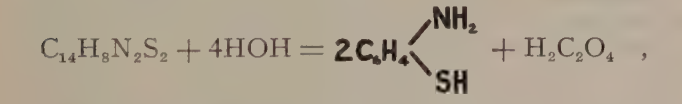
In this paper he further developed two new methods of synthesis which, however, do not admit of general application, by preparing 2 phenylaminobenzothiazole by heating a mixture of anisyl and thioanisyl mustard oils, synthesized by the method of Mülthaüser[19]; and by preparing the oxymethenyl base by distillation of the urethane



which he obtained from the mercaptan and chlorcarbonic ester. During the same year he conducted a research on naphthylthiazoles and prepared a number by methods similar to those already given. (Listed at the end.)

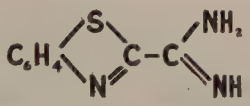
No very satisfactory proof of the structure of these compounds had appeared at any one time, though taking into consideration all the methods of synthesis which had been developed up to this time, there is little doubt left in the mind of even the most critical reader. In 1887,[20] however, Hofmann published a summary of the facts leading to the structural formulae for the thiazoles, using as a case in point, oxalaminothiophenol. Hofmann's proof of the structure of oxalaminothiophenol may be briefly abstracted as follows:

1. Its empiric formula from analysis is $C_{14}H_8N_2S_2$.
2. On hydrolysis it yields ortho-amino-thiophenol and oxalic acid according to the equation:



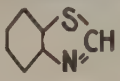
3. It may be synthesized as follows:
   (a) By leading cyanogen into a strong solution of ortho-aminothiophenol

   (b) By adding the mercaptan to an alcoholic solution we obtain amidin as a first product

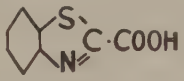


(according to Hofmann) which upon further treatment with the mercaptan yields oxalaminothiophenol. Amidin has two hydrogen

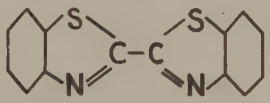
atoms which are easily replaced by phenyl groups and must hence be attached to nitrogen atoms, and on treatment with KOH which would hydrolyze amides gives the potassium salt of an acid which upon liberation of the free acid breaks up into methenyl base. The latter may be synthesized from formanilid and sulphur, from thioformanilid by direct oxidation, and by condensation of ortho-aminothiophenol with formic acid, all of which in consideration of his previous work, lead to the structure of methenyl base as

methenyl base as 

The acid must then have been



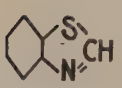
amidin, as given above, and the original base



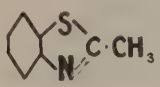
4. Now Bladin[72] working with orthonitroanilin had prepared an analogous series of compounds where the sulphur atom is replaced by an imido group, and had assigned a similar structure to his final product, although he arrived at somewhat different ones for the intermediate amidin and acid, and the formula agreed also with the work of Ladenburg (see previously) and others in related fields, so Hofmann believed his formula to be justified.

At the same time he reviewed the work of Jacobson, and contradicted the latter's statement that he prepared benzothiazole by the oxidation of thioformanilide although he admitted that the ethenyl base could be obtained in this way.

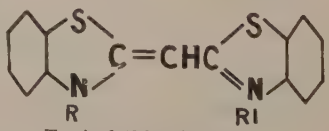
At the end of this paper he made an interesting series of observations and described a few preliminary experiments which should be a very fruitful field for research, and yet which it does not appear that he ever followed up, although he promised to do so. There is a marked resemblance between benzothiazole, methyl benzothiazole, quinolin and quinaldin, as can be seen from the formulae, and it should be possible to obtain from these two a series of dyes resembling the cyanins.



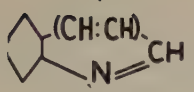
Benzothiazole



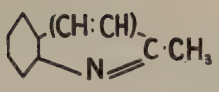
Methylbenzothiazole



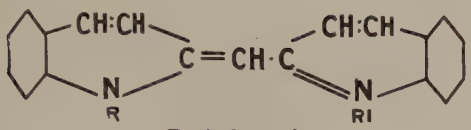
Typical thiazole cyanin



Quinolin



Quinaldin



Typical cyanin

In the cyanines the methyliodide addition products are used and he had already noted that the methenyl base did add methyl iodide, as well as amyl iodide. In a preliminary experiment he condensed the two thiazoles, and each with the other quinolin and did obtain reactions with the formation of dyes but he did not isolate them nor proceed further, nor does it appear that any further work has been done on these compounds.

All of this work, however, had had very little influence on commercial chemistry. Organic sulphur compounds were being manufactured and used as dyes by the Germans, but they were of the phenyl sulphide type described and prepared earlier by Merz and Weith. In February of 1888, A. G. Green,[21] chemist for Brook, Simpson, and Spiller, an English dye concern, found that by fusing paratoluidin and sulphur he obtained two substances which were different from the thiotoluidin of the authors just mentioned, one of which was a direct cotton dye and both of which were primary amines, from which a series of direct cotton dyes could be obtained both by diazotization and coupling, and by substitution. He named these dehydrothiotoluidin and primulin, the latter because it dyed cotton directly a primrose (primula) yellow, and prepared a number of derivatives, the methylated and ethylated bases, sulphonic acids, and several azo dyes, developed a process for producing the azo color directly on the fibre using primulin, and noted that the diazonium compound of the latter was affected by light[22] to such an extent that it would only couple with the developer satisfactorily under certain carefully regulated conditions. Unfortunately, he neglected to patent his work, and as soon as his firm produced them, and the Germans became interested, they found this out, and of course, did not make this mistake. Dahl and Company immediately patented a process practically identical with Green's (D.R.P. 35790) and all of the important work which followed was covered by German patents.

P. Jacobson[23] took up this topic the following year and after a brief review of the patent literature, and of the earlier work of Merz and Weith, Krafft, and Truhlar,[24] he developed a better synthesis of dehydrothiotoluidin and primulin from the same starting materials, using a hydrochloric acid extraction, and sub-

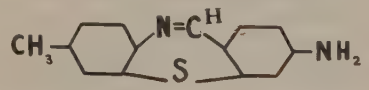
sequent crystallization from alcohol as his method of purification. He described dehydrothiotoluidin as crystallizing in colorless needles, M.P. 190°-191°, and also prepared the phenol, colorless needles from alcohol M.P. 256°, and the acetyl derivative of this, M.P. 132°, crystallizing from alcohol in colorless needles.

During the same year Gatterman[25] investigated the reaction and showed that dehydrothiotoluidin was different from the thiotoluidin of Merz and Weith, although Dahl and Company's original patent described it as such, but his work was not at all enlightening from a structural standpoint. He did make two important contributions, however—he noted that dehydrothiotoluidin formed a dibrom addition product in glacial acetic acid solution, although he did not isolate the product, and suggested naphthalene as a solvent from which primulin could be crystallized for purification. He also investigated the action of sulphur on the other toluidins.

The work of Anschütz and Schultz[26] which appeared at the same time was vastly more important commercially for a great number of patents sprang up from the small space of this paper as a resting place. They studied the action of sulphur on a number of aromatic amines with the following results:

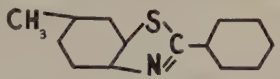
Starting Material	Product	M.P.	Solvent	Form
1. *P*-toluidin	Dehydrothiotoluidin $C_{14}H_{12}N_2S$	191°	EtOH	Yellow needles
acetyl derivative of	"	225°	EtOH	Yellow prisms
2. Amido *m*-xylol	Dehydrothioxylidin $C_{16}H_{16}N_2S$	107°	EtOH	Yellow prisms
acetyl derivative of	"	227°	EtOH	White needles
Noted the formation of a dibrom addition product.				
3. Amido *p*-xylol	Dehydrothioxylidin $C_{16}H_{16}N_2S$	144°	EtOH	Yellow needles
acetyl derivative of	"	212°		
Also forms a bromine addition product.				
4. Pseudo-Cumidin	$C_{18}H_{20}N_2S$	183°	Benzol	Small yellow crystals
	$C_{18}H_{20}N_2S$	125°	EtOH	Yellow needles

Up to this point the structure of the compounds had not been considered except by Green, who assigned to the dehydrothiotoluidin on very little evidence, the structure

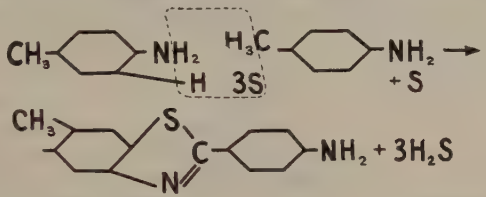


which is not accepted at present. Gatterman and Pfitzinger[27]

now took up the problem. In his previous article just cited, he had prepared

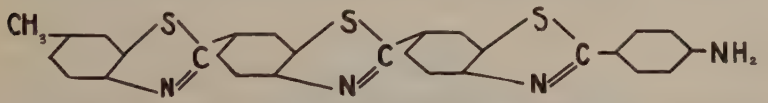


M.P. 123°, by removing the amino group from dehydrothiotoluidin, and he now showed that it was a member of the benzothiazole group and was identical with the product previously prepared by Hess[28] from one of the aminothiocresols and benzoyl chloride. To prove this he synthesized it from thiobenzotoluidid by the method of Jacobson and proved all three products to be the same. By hydrolysis he then split the two substances and showed that they gave the expected acids and aminothiocresol. From this he concluded that dehydrothiotoluidin was formed by this reaction

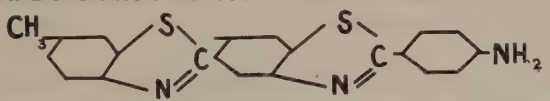


and had the structure given.

The work on primulin was not quite as satisfactory, as it led to two conclusions between which the difficulties of purifying the primulin prevented them from choosing. It may be considered to be formed from two moles of dehydrothiotoluidin similarly to the latter itself which would give the formula



or from one mole each of dehydrothiotoluiddin and paratoluidin which would indicate it to be:

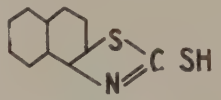


From 1885 to 1890 a great deal of work was accomplished in the thiazole field; Hantsch and Weber,[29] and Möhlar[30] and Krohn prepared the methenyl bases, the latter from methyl and dimethyl anilin and sulphur, while several syntheses of the Rosenkörper were accomplished, from benzalanilin, and benzyl anilin by Ziegler[31] and Wallach.[32] Jacobson's original work on the action of oxidizing agents in alkaline solution on the thioanilides has already been mentioned, and he published a number[33] of articles on this reaction by himself and in collaboration with Ney; as well as on the other reaction he had discovered, namely, that of carbon disulphide on oxyazo linkings to produce thiobenzothia-

zoles, while from 2 thiazole mercaptan by treatment with aniline, Kalkhoff,[34] and Jacobson,[35] separately, and the latter and Schenke (just given) had made phenylaminobenzothiazole.

In 1891 Jacobson and Frankenbacher[36] prepared several new compounds by treating mustard oils with sulphur.

1.

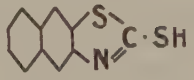


M.P. 240° small colorless crystals from alcohol.

2.

M.P. 194°, crystallizes from benzol and reacts with $HgCl_2$ in alcoholic solution.

3.

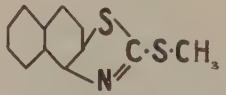


colorless needles from alcohol M.P. 232°.

4.

white needles from $CHCl_3$ M.P. 180°.

5.



colorless needles from alcohol M.P. 74°.

6. Phenylaminobenzothiazole picrate, rosettes from alcohol, M.P. 222°.

7. Phenyl-acetamino benzothiazole, colorless needles from alcohol, M. P. 167°.

All are odorless.

Gatterman and Neuberg[37] in 1891 worked out a synthesis of dehydrothiotoluidin from thioparanitrobenztoluid following out the general method of Jacobson, preparing in the course of the procedure 6 methyl-para-nitrophenyl-benzthiazole but did not describe any of its properties. This was more interesting from a theoretical than a practical standpoint, as the synthesis involved a large number of steps and much material was lost in the course of the reaction.

Research in the field now had reached the point where investigation led to the discovery only of new compounds rather than

of general reactions for the preparation of the thiazoles. O. Kym[38] prepared some of these—6 amino, 2 phenyl-benzothiazole, yellow-green leaves, alcohol, M.P. 202°; the acetyl derivative of this compound white needles from alcohol, M.P. 192°-193°; 6 amino-2 para-aminophenyl benzothiazole, yellow needles from alcohol, M.P. 237°-238°; and the diacetyl derivative of this, reddish-needles from alcohol, M.P. 272°-273°. In 1896 Lauth[39] prepared oxalaminothiophenol, two dinitro, and diamino derivatives whose structures he did not determine, and a number of azo dyes from the latter, while subsequently other special methods for the preparation of Rosenkörper were developed among which may be mentioned that of Voswinkel[40] from benzoyl·phenylhydrazine and sulphur, and Wheeler,[41] from orthoamino-thiophenol and benzimido methyl ether, while Schmidt[42] prepared 6 dimethylamino benzothiazole from dimethyl-paraphenylene-diamine thiosulphonic acid by condensation with formaldehyde and oxidation of the product with nitrous acid. Reissert[43] also did some work on the benzothiazoles, but did not contribute anything new or interesting.

As has already been noted, from a commercial standpoint, the most important compounds of this group are the so-called anhydro-bases which are obtained by the direct fusion of aromatic amines with sulphur, although perusal of the patent literature shows that almost all of the phenyl benzothiazole amines that have been prepared have also been patented. The basic patents in the dye-field are those founded upon the original work of Green and that of Anschütz and Schultz, and all may be classified according to the particular base with which they deal, into groups as follows:

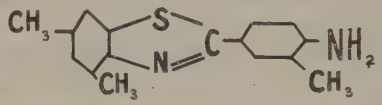
1. Mono or diamino derivatives of 2 phenyl benzothiazole, or 2 phenyl alpha or beta naphthiazole. These are not very important and there are comparatively few patents dealing with them.

2. Dehydrothiotoluidin, 6 methyl 2 para-aminophenyl benzothiazole which, as has already been noted is the most important of all, and a large number of patents deal with its preparation as well as that of its derivatives. The experience of different concerns which have manufactured this base appears to have differed, as may be readily seen from a perusal of the patent literature.[44] The main difficulty has been the separation of the principal product from the primulin simultaneously formed, a problem which has not been satisfactorily solved although it can be done by a vacuum distillation of the fusion mixture, or by means of the difference in solubility of the ammonium salts of the sulphonic acids of the two bases as described by Noetling[45] and in the patent just given (the method was discovered by Hall in 1889). For the preparation of some of the thioflavins the sulphonic acids are undesirable, so this method has a serious objection, as up to date it has not been possible to regenerate dehydrothiotoluidin from its ammonium sulphonate.[46]

From the practical side the application of the dyestuff is as

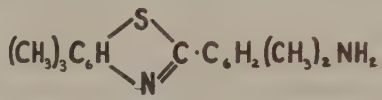
important as its preparation, and some of the methods of substantive cotton dyeing as applied to primulin are discussed by Haller,[47] while in the experimental part of this paper an adaptation of the Badische method which works fairly well for laboratory purposes, is given.

3. Dehydrothioxylidins, of which the commercially important one is the meta compound



prepared as mentioned above by Anschütz and Schultz, and described in the Bayer Patent already given.

4. Dehydrothiopseudocumidin, also prepared by Anschütz and Schultz and covered by the Bayer patent, which, however, does not mention which of the two isomers is meant—



5. 6-Para-aminophenyl dehydrothiotoluidin, prepared from benzidine and paratoluidine and the corresponding tolidine compound, covered by several patents which may be found in the third volume of Friedländer.

6. 6-6 Bisdehydrothiotoluidin, prepared also from benzidine and paratoluidin, and the corresponding tolidine compound, which are really further condensation products of those in group 5.

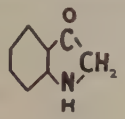
7. Bases of unknown or uncertain structure, such as primulin, the chromins, etc.

From these seven groups a large number of dyes have been made which fall more or less naturally into subdivisions: (1) Those bases which are themselves direct colors on cotton, as for example, primulin and chromin; (2) alkylated bases, or alkylated and sulphonated bases such as thioflavins; (3) substituted bases, nitro derivatives, etc., which are comparatively few, although nitro derivatives of dehydrothiotoluidin have been made and used as dyes; (4) oxidation products like naphthamine yellow produced by the action of bleach on dehydrothiotoluidin, and (5) azo dyes which are by far the greater majority, and can be conveniently subdivided into monoazo and bis-azo compounds, and both of which are represented in larger numbers.

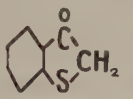
The colors of these dyes are in the main confined to the red-yellow end of the spectrum, although in the derivatives of groups 5 and 6 some blues and greens are found. A series of greens may also be obtained by coupling diazotized dehydrothiotoluidin with the naphthyl-amine sulphonic acids, rediazotizing and treating with dioxy naphthalene disulphonic acids. It is interesting to note in passing that while primulin can be diazotized on the fibre as was shown by Green in his original work, this process

is not possible with dehydrothiotoluidin. These dyes are all direct substantive ones for cotton, are reasonably fast to acid, alkali, and bleach, but as has been noted by all the workers in the field, only moderately so to light, a thing which of course, reduces materially, their value.

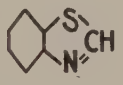
This fact brings up a rather interesting point in connection with structural relationship of organic compounds. The indigoid and thioindigoid dyes are amongst the fastest of all toward light and owe a great deal of their commercial importance to this fact, as well as, of course, to the wide variety of colors that can be obtained from them, particularly in the case of the latter. There is a rather close genetic relationship between some of the thiazoles and the corresponding compounds in the indigo series as may be seen at a glance from comparison of the accepted structural formulae:



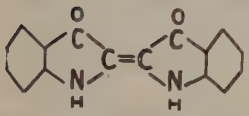
Indoxyl



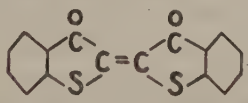
Thioindoxyl
(Thionaphthene)



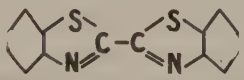
Benzothiazole



Indigo

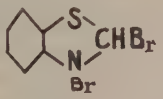


Thioindigo

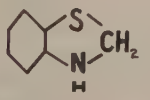


Oxalamido thiophenol

Benzo-thiazole may be regarded as derived from indoxyl by replacement of the carbonyl group with a sulphur atom and removal of the two hydrogen atoms, and oxalamido-thiophenol as bearing a corresponding relationship to indigo. As already mentioned, it has been observed by several workers that the thiazoles form dibrom addition products, and from similar reactions, we should expect the compound which Gatterman did not investigate, to have the formula



and to be reduced to



which would make it resemble indoxyl still more closely, and then reasoning along the same lines, we should be able to obtain the analagous reduced oxalamido-thiophenol both by reduction of the bromine addition product which has not been made, and by oxidation of the postulated dihydro-methenyl base. If the ac-

cepted view of the cause of the color of the indigoid dyes is correct, we should not expect the compound to be a dye.

APPENDIX TO THE HISTORICAL REVIEW

1. Friedländer devotes a chapter of each volume of his work to patents dealing with sulphur dyes, most of which refer to the so-called anhydro bases, and the large majority of them are descriptive of azo or bis-azo dyes. Among the substances with which dehydrothiotoluidin has been diazotized and coupled, may be mentioned by way of example: salicylic acid; beta naphthol; beta naphthol alpha or beta monosulphonic acids; phenols and cresols; itself, primulin, and their sulphonic acids; tetrazodiphenyl or tolyl; napthionic acid; ammonia; metatolylene diamine; beta naphthylamine sulphonic acids; resorcin; oxynaphthoic acid; naphthol disulphonic acids; dyes such as chrysoidin and Bismark Brown; alpha naphthylamine sulphonic acids; Clève's acids further diazotized and coupled with compounds already given; and the aminonaphthols and their mono and disulphonic acids and ethers.

2. To substantiate the conclusions arrived at regarding the second and third purposes of this research, the following partial list of compounds which have been prepared by previous workers together with their properties, in addition to those already mentioned and others which will be described, is given. These are all benzothiazole derivatives and merely the substituting groups and their positions are indicated for the simpler ones.

Groups	M.P.	Odor	Color
benzothiazole	210°	aromatic	none-white
2 chlor	M.P. 24° B.P. 248°	"	"
(?) nitro 2 chlor	192°	none	"
2 hydroxy	139°	"	"
2 ethoxy	25°	aromatic	"
2 acetoxy	60°	none	"
2 amino	129°	"	"
2 phenylamino	159°	"	"
2 methyl	B.P. 238°	aromatic	"
2 ethyl	B.P. 252°	"	"
2 butyl	Not found	not given	"
S2 dibenzothiazole ethane	137°	none	"
p 2 dibenzothiazole benzene	112°	"	"
2 oxymethyl	176°	"	"
2 benzyl	.....	—	"
2 orthohydroxyphenyl	129°	none	"
S-phenyl benzothiazole ethane	111°	"	"
6 methyl	M.P. 15° B.P. 255°	aromatic	"
2, 6 dimethyl	No data		
6 methyl 2 phenyl	125°	none	none
2 phenyl naphthiazole	100—101°	"	"
naphthiazole	45°	"	"
2 methyl naphthiazole	No data		
oxalaminoalphathionaphthol	300°	"	yellow
oxalamino betathionaphthol	.....	"	yellow

EXPERIMENTS

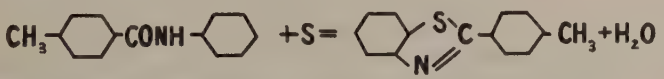
Part A—Benzothiazoles

1. *Oxalamino-thiophenol*

In order to become familiar with the technique of the preparation of these compounds, this synthesis was attempted as a starting point, since it involves a sulphur fusion which may be considered typical. 300 g. of acetanilide was heated with 180 g. of powdered roll sulphur following the directions of A. W. Hofman.[48] The weight of the melt at this point was 282 g., which was then treated according to the directions of Lauth[49] for extracting the pure compound. 60% sulphuric acid, by weight, extracted only 140 g. of the melt corresponding to a 50% yield against 60-70% as given by the original article. Crystallization from boiling aniline yielded a colored product, and as the solubility in ethyl alcohol is less than 1 g. per 100 c.c. and it is equally or more insoluble in ether, nitrobenzene, aniline, amyl alcohol, amyl acetate, and mixtures of these, it was decided that purification by other methods than sublimation was impracticable. Sublimation of 75 g. yielded 7 g. of white, odorless needles, melting at 304° (Unc.), which was then recrystallized from a large volume of ethyl alcohol. The final yield, calculated back, was less than 5% of the acetanilid used, and was considerably less than that given by either of the previous investigators.

The extreme minuteness of the yields proved to be a regular occurrence in all similar experiments and this, as well as the difficulty in obtaining the intermediates required, was a continual source of vexation and a serious handicap to the progress of the work. For this reason the syntheses in each case are given fairly completely to save time wherever it may be necessary or desirable to duplicate or continue the work. The yields described in this dissertation have all been actually obtained and can be duplicated by fairly careful manipulation.

In accordance with the first and third purposes of this research, it was considered desirable to prepare a homologue of the "Rosenkörper" and to determine whether it would exhibit an odor resembling that of the interesting substance obtained by Hofmann. With all the methods, previously enumerated, available, it was decided to attempt the synthesis of 2-paratolyl-benzothiazole which if successful, would be a new contribution to the chemistry of the group, by the original method of Hofmann, which should proceed as follows:



Paratolanilide was required as a starting material and as it was

not available, the synthesis was perforce accomplished from paratoluidin.

2. Paratoluyl Nitrile

This compound was made following the directions of Gatterman[50] and of Fisher.[51] The reaction proceeds as described and the yields and melting points coincide with the accepted ones.

3. Paratoluic Acid

Prepared according to the directions of Gatterman and Fisher as just given. Yield and M.P. were as recorded.

4. Paratoluyl Chloride

As first attempted, a method adopted from Gatterman's[50] preparation of benzoyl chloride was employed. The reaction does not proceed satisfactorily and after two trials it was discarded.

The compound was synthesized by the method of Frankland and Wharton[52] (see also F. and Aston) and the yield was 55-60% of product boiling from 182° C.-185° C. at a pressure of 260 m.m.

5. Paratolanilide

The literature furnishes a number of methods for this synthesis by Wegerhoff,[53] Brückner,[54] Fischli,[55] and Leuckhardt,[56] and the observed melting points vary from 139° C. (Fischli) to 145° C. (Leuckhardt).

Since paratoluyl chloride was available from the previous synthesis, the method of Fischli was selected and modified.

In a one liter flask, dissolve 15 g. (18 c.c.) of freshly distilled aniline in 200 c.c. of water- and alcohol-free ether. From a dropping funnel add slowly with good stirring 25 g. of paratoluyl chloride. The reaction proceeds smoothly according to this equation:

$$CH_3C_6H_4COCl + C_6H_5NH_2 = CH_3C_6H_4CONHC_6H_5 + HCl$$

the product separating out at once as a fine white precipitate. Evaporate off the ether, or better, distill off on a water bath, and dissolve the residue in the least amount of 50% ethyl alcohol, in which the solubility is about 5 g. per 100 c.c., by warming. Allow to cool, filter by suction, and wash with cold water. The yield is practically quantitative and the purity of the product is satisfactory for most purposes. On recrystallization from ethyl alcohol it appears in shining white plates, M.P. 145° C. (cor.).

6. 2-Paratolyl Benzothiazole (A)

The first attempt to prepare this compound was, as has already been mentioned, according to Hofmann's first general method, the fusion of the anilide with sulphur.[57] A mixture of two parts by weight of paratolanilide and one part of powdered roll sulphur was placed in a flask equipped with a reflux air condenser, and kept at a temperature of 290° to 300° C. for two hours on an oil bath. At the end of this time the melt was poured into a beaker, allowed to solidify, and powdered. The weight of the fusion mixture at this point was 1.5 to 1.6 parts in several experiments, and was dark brown in color. It was extracted repeatedly

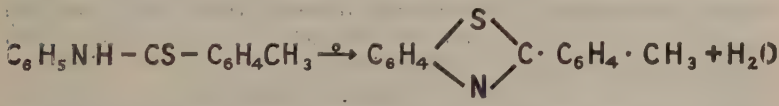
with 100 c.c. portions of concentrated hydrochloric acid (39% HCl by weight, specific gravity, 1.2) and the liquid extract diluted with water, but no precipitate formed. On neutralization with sodium carbonate and long standing, a small amount of yellow material, insufficient to purify, was deposited, and a solution of this in alcohol and in concentrated hydrochloric acid gave a yellow precipitate with 1% gold chloride solution, a reaction which is characteristic of these bases. Alcohol and ether extractions of the melt gave similar results, and it is probable that the yield of the desired substance in the reaction, is positive, but certainly less than 1%.

It was thought, however, that the direct fusion of the two substances might have been responsible for the low yield, due to too powerful oxidation and consequent charring, and accordingly the addition of naphthalene as a diluent was next tried. The melts were made up as follows:

Paratolanilide	12 g.
Naphthalene	12 g.
Roll Sulphur	6 g.

according to the method described later for dehydrothiotoluidin. They were heated for two hours starting at 160° and ending at 200°. At the end of the first hour a marked color change to yellow occurs, but the desired substance was not found in the final mixture.

Hofmann's method for preparing the desired compound having failed, it was next decided to attempt its synthesis analagously to the method by which Jacobson[58] had obtained the "Rosenkörper," for which the reaction should be in this case:



Thioparatolanilide was required as a starting substance and as this was not available, it was again necessary to prepare a number of intermediates.

7. Thiocarbanilide

Prepared from aniline and carbon disulphide according to Gatterman.[50]

8. Phenyl Mustard Oil

This was made from thiocarbanilide as described by Gatterman.[50]

9. Thioparatolanilide

This compound was synthesized by the method of Gatterman[50] whose method is simpler than that of Leo, which has already been mentioned in the introduction. Since the substance was required in fairly large quantities, it was found necessary to modify the original method somewhat, as it is undesirable to

use amounts much larger than those in the above-mentioned paper, because of the tendency of the aluminum chloride to cake, with an accompanying reduction in yield. It is preferable to carry out the reactions in separate vessels. The ensuing directions involve about the maximum quantities with which it is possible to secure satisfactory results, but by running a number side by side, much more can be made without a great increase in the time necessary, and with very good yields.

A mixture of 15 g. of phenyl mustard oil, 30 g. of toluene and 30 g. of aluminum chloride, (anhydrous) is allowed to stand, in a one liter flask with an electric stirrer, on a water bath for two hours, and then to complete the reaction, is left over night. Decompose the solid reaction product carefully with ice water, and distill off the unchanged toluene and phenyl mustard oil with steam. On more than one run this may, of course, be done successively with the same apparatus. The residual liquid in the flask is poured into a beaker and deposits, on cooling, a solid which consists chiefly of the anilide, but contains some alkali-insoluble impurities. Filter off, and if more than one preparation is being made, unite the yields at this point.

Warm the solid material with 10% KOH using 300 c.c. to each run, and filter. Extract a second time, using 150 c.c. to each. (The solubility of the anilide is about 9.2 g. per 100 c.c. in the dilute alkali at 20° C.) Unite the filtrates and neutralize with 20% sulphuric acid. Yield is 80% of the theory and the purity is sufficient for most purposes. (This yield may be cut to 40% simply by using double the quantities directed.)

Thioparatolanilide may be recrystallized from ethyl alcohol, in which the solubility at the boiling point is about 30 g. per 100 c.c., in which it gives a red solution, which on cooling, deposits yellow nedles meltng at 142° C. (cor.).

10. *Paratolylbenzothiazole (B)*

From the compound just described, the new sulphur base was prepared successfully by an adaptation of the method of Jacobson.[60]

In a liter beaker, dissolve 16 g. of thioparatolanilide in 700 c.c. of water containing 60 g. of sodium hydroxide. (An equal weight of potassium hydroxide can be used with the same results.) It is necessary to warm to effect solution. Allow to cool to room temperature and add 227 c.c. of a 20% solution (containing 45 g. of solute) of potassium ferricyanide. The mixture becomes milky yellow at once. Allow to stand twenty-four hours and filter off the resinous precipitate.

Extract twice with 150 c.c. and 100 c.c. of concentrated hydrochloric acid respectively, filtering through asbestos each time. The solid becomes a bright red at first, on addition of the acid. Mix the extracts and drown them in ten times their volume of water. After extraction all but a small amount of material which is an

oil below 100°, but solidifies to a gummy mass, should have dissolved. The precipitate on the addition of water is voluminous and pale yellow in color. The weight is 60-75% of the theory according to the equation given above. There is no advantage in neutralizing the acid with sodium carbonate.

Absolute purity requires several recrystallizations from alcohol, as the impurities though small in quantity are difficult to remove, which finally yields it in colorless, odorless needles, melting at 85° C. (cor.). When slightly moist with alcohol, the new base has a faint odor which is somewhat suggestive of "Rosenkörper," but its intensity is so small as to be barely perceptible.

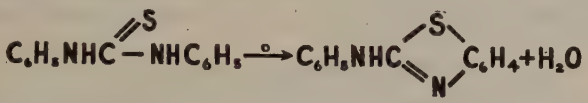
Analysis:

Calculated for $C_{14}H_{11}NS$ N = 6.22%

Found N = { (6.46% / (6.55%

11. 2-*Phenylaminobenzothiazole*

In the light of the synthesis just given, it occurred to the author that the 2 phenylaminobenzothiazole which has previously been prepared by Hofmann and others, should be formed by the oxidation of thiocarbanilid in the Jacobson reaction, according to the equation:



Accordingly the experiment just described was repeated, using the same molecular quantity of thiocarbanilid instead of thioparatolanilide. The precipitate which formed in the oxidation mixture was found to be practically insoluble in concentrated hydrochloric acid, the liquid extract on dilution with water depositing only a trace of gray-white substance which on a single crystalization from ethyl alcohol melted at 144.5° C. (cor.) and may have been the desired compound but the amount was too small to identify. The residue was yellow in color and had lost very little in weight, and from it a substance soluble in alcohol, from which it crystallized in yellow needles melting at 237.5° C., was isolated.

At the end of one of his papers, Jacobson[80] makes a brief reference to having tried this reaction, and mentions carbanilid as one of the products, the other being an amorphous, insoluble material that was not investigated. This may be prepared as follows:

Dissolve by heating, 18.0 g. of thiocarbanilide in 800 c.c. of water to which has been added 60 g. of sodium hydroxide. All will not quite dissolve. Cool and add a solution of 52 g. of potassium ferricyanide in 260 c.c. of water. Let stand 24 hours, filter, and dry. Residue is yellow in color and weighs 16 g.

Extract with 150 c.c. of 95% ethyl alcohol by heating. Filter.

A second extraction is unnecessary. The residue is yellow, weighs 7 g., is highly insoluble in all ordinary solvents, except nitrobenzene, from which, however, it was not successfully crystallized, and is evidently the product mentioned by Jacobson. After some difficulty, his other observation was also verified. The filtrate was allowed to crystallize, and then the product repeatedly crystallized from alcohol, yielding finally a substance melting only slightly below carbanilid but exhibiting a yellow color and giving a qualitative test for sulphur. It was attempted to hydrolyze this compound using 30% aqueous potassium hydroxide, and 20% alcoholic potash in different experiments. Both yielded the same substance, which appeared in white shining needles on recrystallization from ethyl alcohol, melted at 238° C. (cor.), were free from sulphur, and gave the bromine addition product characteristic of carbanilid. (As did also the original substance.) Contrary to the test given by Mulliken[61] carbanilid is apparently not hydrolyzed rapidly by alcoholic potash which does, however, remove the sulphur-bearing impurity. This can also be done by shaking the original material with alcohol in which the carbanilide dissolves more rapidly and leaves a small amount of yellow material, too little to examine, however, at the bottom of the vessel. The extreme insolubility of the first substance made impossible any further investigation of it.

The aniline blues and reds are among the most important of the triphenylmethane dyes and have been prepared in a number of ways, from benzyl chloride, para rosaniline and aniline, diphenyl amine, etc.,[62] and of this group probably the best known is aniline blue itself, to which the structure

$$(C_6H_5NHC_6H_4)_2:C:C_6H_4:N.C_6H_5.HCl$$

is ordinarily assigned. The last mentioned synthesis of this compound suggested, that, since phenylaminobenzothiazole contains a secondary nitrogen group and is structurally closely related to diphenylamine, it would react similarly in the Hausdörfer reaction, yielding upon fusion with oxalic acid, a substance whose probable structure would be

$$(C_7H_4NS.NHC_6H_4)_2:C:C_5H_4:N-SNC_7H_4.$$

Reasoning by analogy, this compound should be a direct silk dye and probably have a color in the blue-green region of the spectrum.

As has been previously noted, phenyl aminobenzothiazole has been synthesized by a number of methods which may be briefly summarized:

(1) From phenyl mustard oil and phosphorus pentachloride, followed by treatment with aniline, by Hofmann.[63]

(2) From anisyl and thioanisyl mustard oils by Hofmann.[64]

(3) By Jacobson and Frankenbacher from phenyl mustard oil and azo-benzene.[65]

(4) By hydrolysis of the dibrom addition product of thiocarbanilid with sodium carbonate, by Hugershoff.[66]

Consideration of the methods available led to the selection of the fourth as being the simplest both from the standpoint of manipulation, and ease in obtaining the necessary reagents, for the difficulty in preparing starting materials was a continually vexatious matter in the course of this research. Accordingly the compound was prepared by the method of Hugershoff which was found to yield the amount of product recorded by him, in a good state of purity, with a great deal of unnecessary labor, a thing which in almost every preparation in the thiazole field was a decided handicap, for many of the reactions which were met with during this work, did not give the yields which the context would seem to indicate, and the problem of purification is always a peculiarly difficult one because of the number and nature of the by-products of the reactions, as well as in many cases the extreme insolubility of the principal substance in most ordinary solvents.

2-Phenylaminobenzothiazole is a colorless, odorless solid crystallizing from ethyl alcohol in small crystals, melting at 161° C. (cor.). As its physical properties as well as the chemical and physical properties of the new dye differ somewhat from those of the corresponding substances in the aniline blue reaction, it was necessary to modify the procedure in order to apply it to the case in hand.

12. *Tri (2 Anilinobenzothiazolyl) Carbinol*

A mixture of 20 g. of phenylaminobenzothiazole and 10 g. of oxalic acid is heated to 170° on an oil bath in a flask equipped with a reflux air condenser and 10 g. more of oxalic acid is added in the course of 15 or 20 minutes. The temperature of the reaction mixture is then raised to 190° and kept there for two hours. It foams at first, probably due to decomposition of the acid, but at the end of the time remains in a state of quiet fusion. Pour into a beaker and allow to cool and solidify.

Grind up in a mortar and extract twice with hot water to remove the excess oxalic acid. The water acquires a slight purple color and a purple mass remains. Dissolve in 150 c.c. of boiling 96% ethyl alcohol and add 5 c.c. of concentrated hydrochloric acid. The dye will not crystallize out on standing, and the solution is evaporated to a gummy paste to which is added 40 c.c. of ethyl alcohol and a solution of 2.5 g. of sodium hydroxide in 20 c.c. of ethyl alcohol. (The last two steps may be omitted as is obvious on consideration, but are recommended for purification.) Heat under a reflux condenser for one hour and allow to stand for 24 hours. A white precipitate settles out and the supernatant liquid is brown in color.

Filter and neutralize to litmus with dilute (1:1) hydrochloric acid. The liquid becomes purple as the neutral point is approached and a small amount of resinous material separates out. Filter this off and reject it.

The filtrate is treated with double its volume of water and allowed to stand one hour before filtering. The precipitate appears to be a mixture of the leuco base and color base and its dry weight is 19 g. or 90% according to the reaction:

$$3C_{13}H_{10}N_2S+H_2C_2O_4=C_{40}H_{26}N_6S_3+3H_2O+CO$$

The melting point is not sharp, but is below 100°.

13. *Di-benzothiazolyl-Fuchsone-Benzothiazolylimine*

The leucobase is then oxidized to the dye with lead peroxide by the method of Gatterman[50] using a suspension of the finely powdered material as it is insoluble. Heat and shake the solution for 15 minutes and filter after adding the sodium sulphate according to his direction. Extract the precipitate with hot ethyl alcohol and precipitate with water.

The new dye has a deep purple color but very poor tinctorial value, dyeing silk only a pale lavender from alcohol solution as it is insoluble in water. This is probably due to the fact that apparently the hydrochloride is unstable and is hydrolyzed by water, for a qualitative analysis showed C, H, N, and S, but no chlorine. It was then analyzed for nitrogen according to the method of Fisher[51] as were the other analyses.

Calculated for $C_{40}H_{26}N_6S_3$ $N = 12.24\%$

Found $N = \begin{cases} 12.03\% \\ 12.12\% \end{cases}$

14. *Sulphonation of the Dye*

It was thought that the poor tinctorial value of the new substance might be due in part to its neutrality and extreme insolubility, so an attempt was made to sulphonate it with 15% fuming sulphuric acid. The sulphonation mixture was diluted with water, neutralized with barium hydroxide, and the precipitated barium sulphate was filtered off. The resultant yellow solution was concentrated and allowed to crystallize, depositing pale yellow plates, but as the hue of the dye appeared to be destroyed in the process, no further work was done on it.

15. *Nitro-tolyl Benzothiazole*

In connection with the second and third purposes of this investigation, it was considered desirable to prepare some of the derivatives of the paratolyl benzothiazole especially the nitro ones, because the nitro group frequently functions as an odorophore, as in the synthetic musks; and the amino derivatives, which would be isomeric with the valuable dehydrothiotoluidin which has already been mentioned a number of times.

The nitration of paratolyl benzothiazole may be accomplished with fuming nitric acid or a 1:1, by volume, mixture of concentrated sulphuric and nitric acids. The best procedure for moderate quantities follows:

In a small flask dissolve 2.5 g of paratolylbenzothiazole in 10 c.c. of concentrated sulphuric acid and add 10 c.c. concentrated nitric

acid. The solution becomes warm at once, nitrogen tetroxide is evolved, and the color changes from yellow to reddish-brown. Heat on a water bath for one hour. Let cool and pour into 100 c.c. of water. A bright orange-yellow precipitate settles out, which on drying weighs 3 g. The colored impurities may be removed by warming on a water-bath with about 50-80 c.c. of ethyl alcohol, and the residue can then be dissolved in 50 c.c. of hot toluene, which on cooling deposits the mono-nitro derivative in pale cream-colored, odorless crystals, M.P. 219.5° C. (cor.).

Calculated for $C_{14}H_{10}O_2N_2S$	N = 10.38%
Found	N = (10.51% (10.56%

The nitration proceeds smoothly and quantitative yields according to the equation

$$C_{14}H_{11}NS + HNO_3 = C_{14}H_{10}O_2N_2S + H_2O$$

may be obtained from any weights. Toluene is a remarkably good solvent for purification, as the difference in solubility with temperature is strikingly great.

16. *Aminotolyl Benzothiazole*

The nitro derivative was then reduced using zinc or tin and hydrochloric acid according to the method of Gatterman.[50] The amine forms an addition product with the metallic salts from which it is a little difficult to remove the metal, and may be crystallized from ethyl alcohol, amyl alcohol, or toluene, none of which are good solvents as the substance is quite insoluble, but the last is the best of the three, and yields the base in small brown crystals, which are much lighter in color on pulverization and melt at 229° C. (cor.). Amyl alcohol and toluene solutions exhibit a bluish-green fluorescence which is characteristic of most of the benzothiazoles.

Calculated for $C_{14}H_{12}N_2S$	N = 11.67%
Found	N = (11.90% (11.80%

17. *Azo Dyes from Amino Paratolyl Benzothiazole*

Amino paratolyl benzothiazole is not a dye but can be diazotized on the fibre and coupled with the usual materials and yields a series of direct cotton colors. This was done according to the method which will be described later, with the results noted in the table. With the amines as couplers, the developer was made up as a 2% solution by weight, using sufficient glacial acetic acid to dissolve them, and after the cloth was immersed, the bath was neutralized with 10% NaOH, thus precipitating the dye out in the fibres of the material. Other acids do not appear to give satisfactory results.

TABLE

Base diazotized and coupled with:

Coupler		Color	Depth
1. Phenol		Yellow	Good
2. Aniline		"	Fair
3. *p*-Cresol		Salmon orange	Good
4. Para-toluidin		Yellow	Fair
5. *B*-naphthol		Pink	Good
6. Alpha-naphthylamine		Brown	"
7. *B*-naphthylamine		Orange	"
8. Resorcinol		Yellow-brown	"
9. Benzoylene urea		Orange-pink	Poor
10. (2) diazotized	+ resorcinol	Yellow-brown	Good
11. (2) "	+ B naphthol	Orange-pink	"
12. (2) "	+ *p*-toluidin	Yellow	"
13. (12) "	+ B naphthol	Orange red	"
14. (6) "	+ anilin	Brown	"
15. (6) "	+ phenol	"	"
16. (7) "	+ phenol	Orange	"
17. (7) "	+ aniline	Orange red	"
18. base "	+ phenylaminobenzo-thiazole	Yellow-brown	Poor
19. " "			
20. (6) "	+ ammonia	Yellow	"
21. (7) "	+ B naphthol	Purple	Good
22. (6) "	+ B naphthol	Orange	"
	+ p cresol	Brown	"

These colors are all as fast to light, soap, bleaching, etc., as the corresponding azo colors from dehydrothiotoluidin, and the tinctorial value in general appears to be much better, particularly of the browns, where it is really quite remarkable. To put it colloquially, "a little will go a long way." The specimens were all dyed from a 1% solution of the amine in the presence of sodium chloride according to the method given later, dried, and steam pressed.

The bis-diazo compounds are better than the primary diazo ones, both from a consideration of variety, and of depth of color, particularly those of alpha and beta-napthylamines from which, as well as those given, a good series of browns may be obtained. It would be interesting and illuminating to determine if a series of greens could be obtained from this base by diazotizing and coupling with dioxynapthalene disulphonic acids, as in the case of dehydrothiotoluidin,[67] but unfortunately, the last two reagents were not available, and all other attempts to prepare a green or blue failed, with the exception of the one purple found in the chart, which, however, it is interesting to note, begins to approach these in structure.

18. *Para* (2 *Benzothiazolyl*) *Benzoic Acid*

Paratolyl benzothiazole contains a methyl group which it should be possible to oxidize to the corresponding carboxyl group by methods analogous to other side chain oxidations. This was first attempted by means of potassium permanganate in neutral solution in the presence of magnesium sulphate according to Fisher.[51] The permanganate was reduced, but the final yield of the ex-

pected acid from 5 g. of the thiazole was so small that it could only be crystallized once and the amount was too small to proceed further with. The substance obtained was yellow white in color and appeared to decompose, but did not melt up to 270°.

A second experiment was performed using permanganate in alkaline solution, according to the method of Bigelow,[68] and while the yield was larger than in the first case, .5 g. from 5 g. sample, it could not be purified sufficiently, for analysis. The substance resembled that in the first experiment in every way, crystallizing in microscopic white needles from alcohol, which darkened but did not melt up to 270° C.

19. *Primulineazo-Benzoylene Urea*

It has been shown[69] that 1:3 dioxyquinolin is particularly suited, in combination with primuline diazotized on the fibre according to the process invented by A. H. Green, to give acid, light, and wash fast orange colors on cotton. The procedure is given in the patent, for example: one requires for a 2% primulin developed color, a mixture of 1% 1:3 dioxyquinolin as the sodium salt, and 1.5% sodium carbonate in which the material is immeresd after coming from the diazotizing bath. Dioxyquinolin gives a clear orange color of greater acid-, base-, and wash-fastness than the corresponding phenol or resorcin developed colors. It was therefore thought that benzoylene urea which resembles dioxyquinolin closely, would also couple to give a dye exhibiting these valuable properties.

The procedure used in dyeing was a modification of that described in the Badische Co. Pocket Guide, (p. 101), and as practical methods of this kind are not as readily accessible as might be thought at first, a brief summary is given.

(*a*) Before dyeing, boil the cotton in a water solution of sodium carbonate and wash with water.

(*b*) Enter the cotton into the dye bath (2% primulin) and work at a boil for 1½ hours adding 5-30 lbs of crystalline Glauber's salt or 2½ to 10 lbs. of sodium chloride for 100 lbs. of cotton.

(*c*) Dye cotton as just given and treat for one-half hour in a fresh, cold diazotizing bath, using 3 lbs. of sodium nitrite and 8½ lbs. of concentrated hydrochloric acid per 100 lbs. of cotton, keeping the temperature below 50° F. by the addition of ice. Add the sodium nitrite to the acid, not vice versa. (This is an unnecessary precaution for laboratory procedure.) Rinse once in cold acidified water and enter into the developer for one hour.

(*d*) A typical developer bath (for ingrain red) consists of a 1% solution of beta napthol dissolved in warm water by means of an equal weight of sodium hydroxide.

For small amounts of material a 100 c.c. working modification of this gives very good results. The diazotizing bath consists of 17 c.c. of concentrated hydrochloric acid, 6 g. of sodium

nitrite, and 200 c.c. of water. The primulin in this experiment was a museum specimen furnished by the Casella Co., the benzoylene urea was a portion of that prepared by Scatchard,[70] and for purposes of comparison ingrain red (primulin-azo-beta-napthol) was used. Benzoylene urea as a developer gave a yellow brown color that comes out much more slowly than the red.

Tests for fastness were made with these results:

Test	B.U. Yellow	Ingrain Red
Boiling with 5% HCl	Fast	Fast
Boiling with 10% NaOH	Darkens slightly	Bleeds out
Bleaching powder	Not bleached	Not bleached
Direct sunlight—two weeks	Fades slightly more than red	
Soap solution, boiling	Fast	Fast

The tinctorial value of the new dye is just as good as ingrain red, and it appears to be of about the same order of fastness as the latter, except to prolonged exposure to light, but this is more than counterbalanced by its greater fastness to alkali.

Part B—Dehydrothiotoluidin

This compound is prepared commercially, directly from paratoluidin and sulphur, and the methods are at variance on two principal points, the manner of conducting the fusion which is either by a mixture of only the two substances in molecular quantities, or by the addition of a diluent such as napthalene or an excess of partoluidin, and the method of purification. In any event, much primulin and other substances are formed simultaneously, and their formation is greater in the presence of an excess of sulphur, and since dehydrothiotoluidin is the more valuable of the two, this is to be avoided. Of the patents already mentioned[44] the basic ones are those of Kalle and Co., of Biebrich am Rhein (a duplicate of the original one mentioned earlier with some changes), and of Leopold Casella and Co. Three methods of separation of the mixed bases which form the melt are available. The Casella patent appears to do so by a difference in the basicity of the two compounds, claiming that dehydrothiotoluidin is more soluble in a 30% by weight solution of sulphuric acid, while the Kalle patent effects this result by taking advantage of the fact that the ammonium salt of dehydrothiooluidin sulphonic acid is less soluble in water than the corresponding derivative of primulin. The third method consists in distilling the melt in vacuo by which only dehydrothiotoluidin comes over, but from a commercial standpoint this method is unsatisfactory, and although it is being used at present, if there was a way of avoiding it, it would be abandoned due to the difficulties of the process in the plant.

Preliminary experiments showed that, in spite of the number of patents and the volume of literature on this subject, practical directions for the synthesis were noticeably lacking, and a critical study of all the methods was made with a view to supplying this deficiency from a laboratory standpoint, at least.

1. *The Casella Method*

The melt was prepared according to the patent directions in each case, substituting grams for "parts" in the wording of the patent. After heating, the fusion mixture was repeatedly extracted with 500 c.c. portions of 30%, by weight, sulphuric acid until nothing further was dissolved. The liquid extract was then drowned in water, or later diluted only a little more, and neutralized while warm with sodium hydroxide, which precipitates the mixed bases in a form which is more readily filtrable. The first factor investigated was the effect of length of heating time on the weight of the sulphuric acid extract, and it was found that there was very little advantage in keeping the melt in fusion longer than four hours. In extracting the melt it is desirable to keep the temperature below 100° C. on a water bath, when two extractions will remove all of the soluble material with a minimum of impurities. The yield at this point, however, after a number of experiments, was never better than 33% of the theoretical amount of the substance from the equation:

$$2C_7H_7NH_2 + 4S = C_{14}H_{12}N_2S + 3H_2S$$

assuming the extract, for purposes of calculation only, to be pure dehydrothiotoluidin.

It was then attempted to purify the product by recrystallization from solvents. The melting point of the crude extract varies from 165°-175° C. (uncor.). A single crystallization of this from alcohol will bring the melting point up to 185°, and if this is then dissolved in the least amount of hot acetone, refluxed with boneblack for one-half hour, filtered, and allowed to crystallize, a pale yellow product in small needle crystals melting at 192° C. (cor.) is obtained.

There are two difficulties in this method. In the first place the losses by the two crystallizations are so great that it is not a satisfactory method of preparation even from a laboratory standpoint. The first one from ethyl alcohol must be done rapidly from the hot solution as it colors up and becomes tarry and resinous quickly, and purification by crystallization is then impossible, so that of all of the extract can not be utilized. In the second place the composition of the sulphuric acid extract seems to be decidedly variable depending on the physical conditions during the extraction, so that there is frequently some difficulty in getting the first solution to crystallize at all, as dehydrothiotoluidin does not do so in the presence of large amounts of the higher primulines. It was first thought that this difficulty was due to the presence and oxidation of paratoluidin which can be shown to be present in considerable quantities even after eight hours heating. (If the sulphuric acid extract, instead of being neutralized with sodium hydroxide as in the later experiments, is diluted with ten times its volume of water, the bases are com-

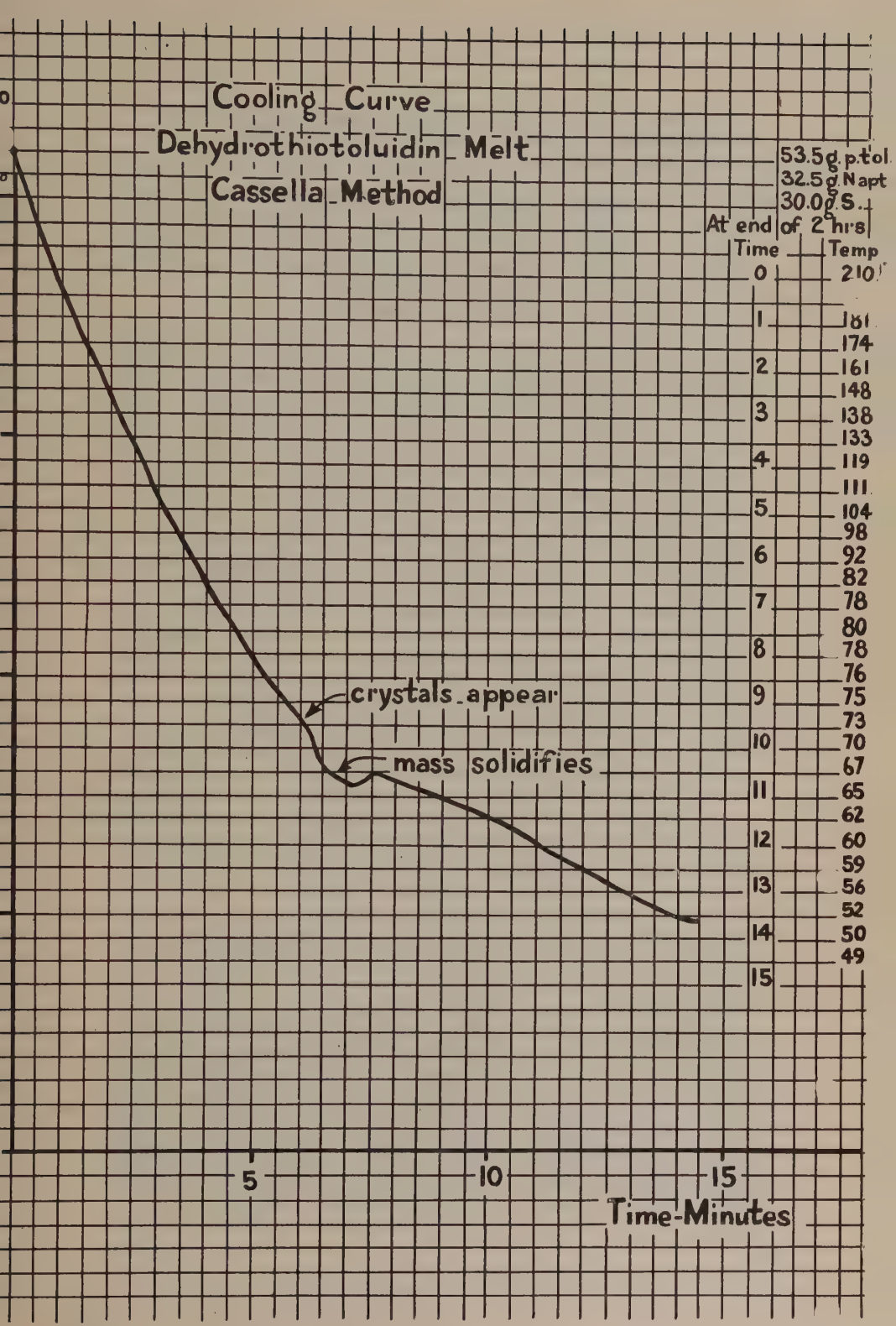
pletely precipitated and the filtrate will deposit nothing on further dilution, but if it is then neutralized with sodium hydroxide, a copious, flocculent, white precipitate is formed which can readily be shown to be paratoluidin.) The idea then presented itself of freeing the mixed bases obtained from the sulphuric acid from paratoluidin by steam distillation before attempting to purify the dehydrothiotoluidin by crystallization, but it was found that this did not solve the problem as the paratoluidin apparently was not responsible for the difficulty. It was subsequently found in the literature that the same suggestion was made by Jacobson[71] in one of the earlier articles, and upon experiment he reached the same conclusion. It was also found by experiment later that pure dehydrothiotoluidin can readily be separated from moderate amounts of paratoluidin by crystallization.

If the second crystallization is made from cold acetone and the boneblack omitted, the substance crystallizing out is dark brown and gummy, does not melt up to 220°, and can not thereafter be obtained as light in color as the preceding product, exhibiting, even after a prolonged boneblacking an orange-yellow color and slightly lower melting point.

2. *The Kalle Method*

It was observed that the relative amount of napthalene as required in the Casella Method could be varied greatly, without affecting the yield. (In order to determine whether there was compound formation between the napthalene and the other substances in the melt, a cooling curve was taken, which indicated that there was not, as may be seen from the diagram.) The napthalene was then omitted entirely, the fusion being carried out as directed in the Kalle patent, but extraction was still used for purification, and the yields and results were the same as those just described. It was therefore concluded that the claim that the use of napthalene increases the yield is unfounded, its only advantage being as a temperature regulator.

The method of purification by vacuum distillation was next tried in a preliminary way. For this purpose melts prepared by the Kalle method as well as samples of the crude material made similarly by the DuPont Co., were used. These melts distilled around 345° C. at a pressure of 35 m.m. and yielded a product which on a single crystallization from alcohol appeared in very pale yellow, odorless needles which on further recrystallization from ethyl alcohol were finally obtained at a constant melting point of 194.8° C. (cor.). This was undoubtedly pure and probably the purest sample of the compound which has been prepared up to this time. The procedure is a difficult one to carry out, the yields here were less than 20% of the weight of the starting material, and the distillation was accompanied by much foaming and decomposition, the greater part of the starting material remaining in the flask as coke at the end. As this


Cooling Curve
Dehydrothiotoluidin Melt
Cassella Method
53.5g. p.tol.
32.5g. Napt
30.0g. S.
At end of 2 hrs
Time Temp
0 210
1 181
174
2 161
148
3 138
133
4 119
111
5 104
98
6 92
82
7 78
80
8 78
76
9 75
73
10 70
67
11 65
62
12 60
59
13 56
52
14 50
49
15
crystals appear
mass solidifies
5
10
15
Time-Minutes

was, however, finally concluded to be the only feasible method of purification, the complete details will be given later.

3. *Attempt to Develop a New Synthesis of Dehydrothiotoluidin*

The work done on the compound up to this point led to the conclusion that in order to prepare a quantity of the substance sufficient for further investigation, and in a satisfactory state of purity, a new synthesis would be highly desirable. The criteria for this reaction as a laboratory problem are:

(*a*) Simplicity of mechanical operations.

(*b*) Large yield.

(*c*) Avoidance of the formation of primulin which prevents the satisfactory crystallization of the compound without introducing large quantities of other by-products.

(*d*) Availability of starting materials. From consideration of the general methods by which thiazoles have been prepared, the following proposed syntheses are obvious at once:

(*a*) Condensation of para-amino-meta-thiocresol with para-amino-benzoyl chloride.

(*b*) Fusion of para-amino-benz-para-toluidid with sulphur.

(*c*) Oxidation of thio-para-amino-benz-para-toluidid with potassium ferricyanide.

(*d*) Fusion of paranitro-benzal-paratoluidin with sulphur analagously to the patent method for preparing "Rosenkörper."[73] It was hoped that in this reaction, if it occurred at all, the hydrogen sulphide formed would reduce the nitro group to the amine, otherwise a final reduction would be necessary. This method was chosen as the easiest to perform because it is readily seen that the required Schiff's base should be easily obtained by condensation of paratoluidin and paranitrobenzaldehyde. This expectation was justified and the compound was prepared just before the publication of the article by Lowy and King[74] on the condensation products of paranitrobenzaldehyde in in which it is described.

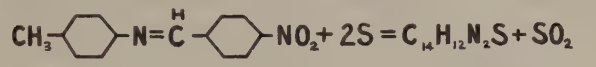
4. *Para Nitro Benzal Paratoluidin*

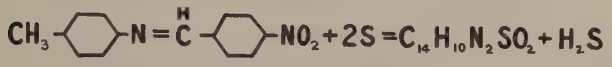
Large quantities of chromyl chloride were prepared by the method of Law and Perkin,[75] and paranitrobenzaldehyde by that of V. V. Richter.[76]

Molecular quantities of the two substances, paratoluidin and paranitrobenzaldehyde, are dissolved separately in the least amounts of 95% ethyl alcohol and refluxed for one hour after mixing. The solution is evaporated to a small volume, allowed to crystallize, and the product filtered off and recrystallized from ethyl alcohol. Paranitrobenzal-paratoluidin appears in pale yellow needles melting at 123° C. (cor.). The yield is only about 50% of the theoretical in a pure state as it is very soluble in alcohol and the losses during crystallization are large.

5. *Fusion of Paranitro-Benzal-Paratoluidide with Sulphur*

It was expected that on fusion with sulphur this compound would behave in one of two ways, or perhaps, both, as follows:





resulting either in the formation of dehydrothiotoluidin or the corresponding nitro derivative.

Accordingly 16 g. of the Schiff base and 4 g. of powdered roll sulphur were mixed intimately and fused on an oil bath in a flask equipped with a reflux condenser for 1½ hours at 200° C. Vigorous ebullition occurred almost at once and sulphur dioxide was evolved rapidly. The mass became viscous at the end of three-quarters of an hour and was almost entirely solid, at the end of one hour. Allowed to cool, broke the flask and pulverized the melt, which was black in color and weighed 16 g. It was then extracted twice with concentrated hydrochloric acid in 100 c.c. portions which were diluted with water, neutralized with sodium hydroxide and filtered. The acid solution changed from yellow to a milky purple at the neutral point. A small amount of purplish-brown material, the dry weight of which was less than 1 g. was obtained. The mass appeared to have charred to a large extent and the yield was too small to proceed further with. It was not dehydrothiotoluidin or the nitro compound, and resembled the product obtained later from nitrotoluene in every way.

It was thought that a lower temperature might improve the results, so the experiment was repeated using xylenes as a diluent and temperature regulator.

A mixture of 12 g. of paranitro-benzal-paratoluidin, 55 c.c. of xylenes, and 3 g. of sulphur, was refluxed for 5 hours, the mixture was then diluted with water and steam distilled, and the xylene recovered from the distillate. The residue in the flask consisted of a dark brown solid and a yellow substance, more of which is deposited in yellow needles from the water solution on cooling. Filtered and separated the yellow needles from the brown material which was present in large lumps. None of the starting material was obtained from this, although the brown mass did contain free sulphur. The products of the reaction were the brown, amorphour, insoluble material, and the yellow crystals, which are soluble in alcohol from which they crystallize in small crystals of indistinguishable shape, melting at 227-228° C. (cor.). The water solution of this compound is acid to litmus, qualitative analysis showed the presence of carbon, hydrogen, and nitrogen, and a sample gave the reduction test for the nitro group. It was not investigated further as it was evidently not the desired sulphur base.

6. *Fusion of Paranitrotoluene and Sulphur*

At this point the thought suggested itself that paranitrotoluene should yield dehydrothiotoluidin or its nitro-body on fusion with sulphur by reactions similar to those already given.

(*a*) $2CH_3.C_6H_4NO_2 + 2S = C_{14}H_{12}N_2S + SO_2 + 2H_2O$

(*b*) $2CH_3.C_6H_4NO_2 + S = C_{14}H_{10}N_2SO_2 + 2H_2O$

A mixture of 30 g. of paranitrotoluene and 15 g. of sulphur was heated under a reflux condenser and for two hours sulphur dioxide was evolved vigorously. The melt which on cooling weighed 29 g., was powdered and extracted three times with 100 c.c. portion of concentrated hydrochloric acid which were then drowned in ten times their volume of water. On standing a dark brown flocculent precipitate settled out, and was filtered off and dried. It blackened up somewhat on standing, and weighed 7 g. when dry. The extract was pulverized and warmed with 100 c.c. of ethyl alcohol, filtered and the deep red solution was evaporated down and allowed to crystallize, yielding about a gram of light brown micro-crystals that appeared to sublime or decompose around 230° C. Qualitative analysis showed the presence of carbon, hydrogen, nitrogen, and sulphur. Zinc dust in 50% ethyl alcohol appears to react with the substance as it gives a yellow solution with a pale green fluorescence, but the reaction mixture does not reduce ammoniacal silver nitrate and consequently the original substance is not a nitro compound.

Gatterman and Neuberg[17] prepared dehydrothiotoluidin from thio-paranitro-benztoluid by the Jacobson reaction. They describe the nitro compound as crystallizing in yellow-red needles from glacial acetic acid, and none of the above mentioned substances resembles, even slightly, this or dehydrothiotoluidin.

The substance obtained in this reaction is a sulphur compound, probably identical with that obtained from para-nitro-benzal-para-toluidid, has some tinctorial value, and does not correspond to any that have been prepared. As it can be made easily in moderately large quantities, it might be worth while to investigate the reactions further, but, as for the preparation of dehydrothiotoluidin, these experiments failed, this was not done.

7. *Apparatus for the Vacuum Distillation of Dehydrothiotoluidin*

After attempting to prepare the compound in fairly large quantities by all of the known methods, and unsuccessfully trying to develop a new one, it was finally concluded that the Kalle method offered the only possibility, and purification must be accomplished by vacuum distillation. Preliminary work showed that the difficulties were mainly low yields and the tendency of the compound to swell up and run over during the process of distillation making it impossible at first to obtain more than 10 g. of the compound by this method in a single operation on a laboratory scale.

The apparatus first tried was the ordinary vacuum distillation set up. At the lowest pressures obtainable with a good water

Vacuum Distillation Apparatus

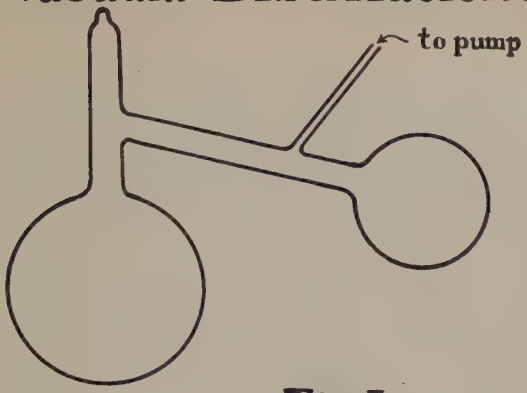


Fig. I

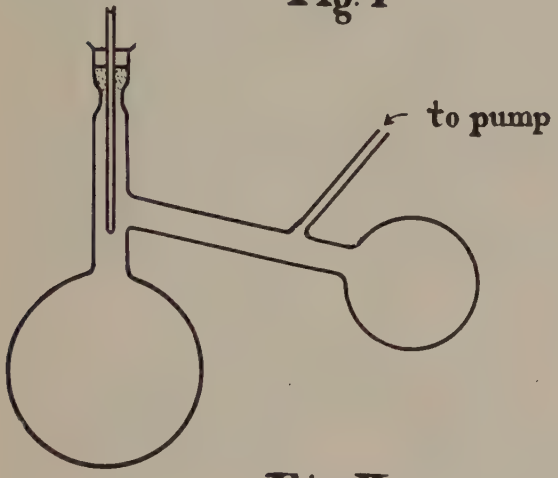


Fig. II

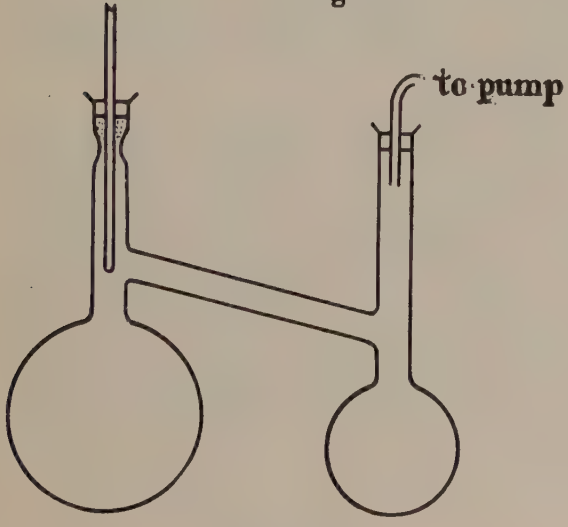


Fig. III

pump (20-30 m.m.), dehydrothiotoluidin distills around 350° C., and it was found impossible to maintain a good vacuum at this temperature, using cork stoppers with the additional difficulty of more rapid decomposition as the pressure rose, while further, the narrow tube clogs up almost at once. The first step was to modify the apparatus as shown in the diagram (Fig. 1), the flasks being 250 c.c. Pyrex ones sealed together, and then the whole apparatus was sealed up after the insertion of the mixed bases. The heating was done over a free flame. This had the disadvantage of ordinarily only being capable of one run of 50 g. of mixture (if more is used it will run over, because of the foaming and decomposition), as it requires too great a degree of manipulative skill to cut off the different parts at the end of the operation and then to seal them together again, it being less trouble to make a new apparatus, and in addition the closed arrangement did not give sufficient control of the run.

The next improvement (Fig. 2) was to draw out the neck of the distillation flask, pack the upper part with asbestos, and then close with a rubber stopper, through which a thermometer can be inserted, which is protected from the heat by the asbestos. This was a decided advance, as two or three successive small amounts (50 g.) of mixed bases can be placed in the main flask and distilled before it is necessary to break the apparatus to remove the yield, which disadvantage still remains.

The final and best type of apparatus is shown in Fig. 3. The distillation flask is a 500 c.c. Pyrex one connected to a 250 c.c. receiver by a 6-inch length of Pyrex tubing of the same bore as the neck of the smaller flask. The set-up is evacuated through the neck of the receiver and it is strongly recommended to place a U-tube of cotton wool between the safety bottle and the water pump during distillation, as otherwise, in spite of the best of cooling, the vapors will be carried along and clog up the water pump during distillation, and while this is being remedied there will be much loss of yield due to charring. Cooling is accomplished by immersing the receiver in a water-bath.

In this apparatus 100 g. (not more!) of the mixed base can be distilled at one run, yielding after crystallization of the distillate once from 96% alcohol 22-25 g. of pure dehydrothiotoluidin. To avoid overheating, the distillation flask was heated in a sodium nitrate bath but this was discarded as it was too difficult to control the foaming which inevitably accompanies the operation. If the distillation is done rapidly with a large free flame which also heats the delivery tube, this can be readily done by removing the flame and increasing the pressure judiciously from the stop-cock of the safety bottle when the melt appears to be about to run over, and when it has subsided distillation can be continued.

The advantages of this apparatus are as follows:

(1) The pure dehydrothiotoluidin can be easily removed by running hot alcohol through the delivery tube into the receiver by means of a rubber tube inserted into the neck of the distillation flask, which loosens it up, and it can then be broken up by shaking, and careful manipulation of a glass rod, and taken out.

(2) The apparatus can then be readily cleaned by soaking in hot concentrated sulphuric acid and so can be used repeatedly.

(3) The product obtained is pure and in good quantity, and the decomposition which accompanies the distillation can be controlled as all parts of the apparatus are accessible at all times.

8. *Preparation of Pure Dehydrothiotoluidin*

As a result of the work described, the following procedure for the preparation of the pure compound was arrived at. This method unlike any of the previous ones found in the literature, is complete as far as laboratory directions are concerned, will work exactly as recorded, and was used for the preparation of considerable quantities of the pure base.

110 g. of paratoluidin and 60 g. of powdered roll sulphur are heated from 4 to 6 hours in a one liter flask equipped with a reflux air condenser on an oil bath at 220°. At the end of this time the melt is poured out into an evaporating dish or a mold made of the lid of a flat paper or wooden box, and powdered after cooling. It should weigh about 100 g., depending on how much can not be poured from the flask, but not more than this is used in the subsequent distillation.

The distillation is then conducted in the apparatus in Fig. 3 following the directions and precautions already given. The product is recrystallized once from 96% ethyl alcohol which gives 22-25 g. of yellow needles melting at 192-193° C. (cor.). Further recrystallization and boneblacking will yield it still paler in color and melting at 194.8° C. (cor.) as already described.

9. *Benzal-Dehydrothiotoluidin*

To a saturated solution of dehydrothiotoluidin in alcohol, add the calculated amount of benzaldehyde from the equation:

$$C_{14}H_{12}N_2S + C_7H_6O = C_{21}H_{16}N_2S + H_2O$$

Heat to boiling for a few minutes and allow to stand to crystallization. The yield is practically quantitative and this method may be conveniently used to recover the base from the solutions remaining from its purification, as the condensation product is much less soluble in 96% ethyl alcohol than the dehydrothiotoluidin itself. Recrystallize the product from alcohol in which it gives a pale yellow strongly fluorescent solution, and from which it appears in very pale yellow, odorless, glistening plates melting at 193° C. (cor.).

Calculated for $C_{21}H_{16}N_2S$	$S = 9.76\%$
Found	$S = 9.80\%$

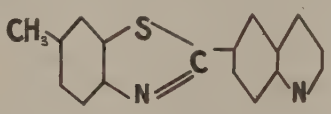
10. *Dehydrothiotoluidin in the Atophan Reaction*

Dehydrothiotoluidin being a primary amine should condense with benzaldehyde and pyruvic acid to give a methyl benzothiazolyl atophan similarly to the reaction which Döbner and Giesiecke[78] found that aniline underwent. The reaction was therefore tried following this method but substituting the molecular quantity of the sulphur base for the aniline. The benzaldehyde condensation product was isolated from the reaction mixture, but no new compound corresponding to atophan was found, although small amounts of an amorphous brown material soluble in toluene, but insoluble in sodium carboniate and hydroxide, were formed.

The experiment was repeated using the benzal-dehydrothiotoluidin instead of the two substances individually, but after 24 hours' heating practically all of the material was recovered unchanged, although small amounts of an amorphous, highly insoluble brown material were formed. Dehydrothiotoluidin apparently will not condense to form a substituted atophan.

11. 6(6-*Methyl Benzothiazolyl*) *Quinolin*

Like other primary amines, dehydrothiotoluidin should condense with glycerine in the presence of sulphuric acid and an oxidizing agent such as nitrobenzene,[79] arsenic acid,[80] ferric sulphate,[81] etc., to yield a quinolin of the structure:



if the reaction proceeds analagously in this case.

The method of Skraup[79] was first used, it having previously been found[82] that practically no quinolin results from reaction of the reduced nitrobenzene during the reaction. 56 g. of crude Casella dehydrothiotoluidin and proper molecular quantities of the other substances, were heated according to the directions. The reaction mixture turned red at once, and a reddish, oily tar formed on the surface as the reaction proceeded, a yellow solid forming on the bottom toward the end of the reaction when the mass became very viscous and boiling slowed up. The mass solidified on cooling, 300 c.c. of water were added and it was distilled with steam to remove the nitrobenzene. The residue in the flask was neutralized with warm sodium hydroxide, filtered and dried, and distilled in vacuo, as it was expected that the new compound would probably be a solid because of its high molecular weight, and complex structure, a conclusion which was later justified. A small amount of yellow solid distilled over with a vile smelling liquid. The solid was filtered off and dissolved in concentrated hydrochloric acid from which it was precipitated with water. It was recrystallized from hot alcohol, and the red, fluorescent solution deposited small light brown crystals (1 g.),

with a tobacco-like odor, melting at 142° C. (uncor.)

The use of the crude dehydrothiotoluidin was thought, however, to offer too many other possibilities, so the reaction was repeated using pure material, and following the method of Kneuppel, with appropriate modifications for the different physical properties of the new substance, which was expected to give a better yield.

15 g. (.07 moles.) of pure dehydrothiotoluidin is dissolved in 20 c.c. of concentrated sulphuric acid which is slightly more than the amount necessary in the original method but is required because of the physical properties of the amine, and 21.7 g. of glycerine and 10.6 g. of arsenic acid were added to the solution in a one liter flask equipped with an air condenser. The large flask is necessary because the reaction is vigorous and the mixture foams up and will run all the way up the condenser otherwise. The mixture is heated, is red at first, but vigorous ebullition soon begins and continues even if the flame is removed, and turns brown as the reaction proceeds, the mixture foaming up. The temperature is kept constant at 190° by means of an oil bath. Stop heating after 1½ hours, cool and add 500 c.c. of water. Continued shaking gives a deep brown solution that appears homogeneous.

Neutralize with solid sodium hydroxide. The solution becomes light brown at the neutral point and deposits a black, tarry material, which is involatile and can not be distilled with steam.

Filter off and dry the black solid. Distill in vacuo in the apparatus designed for dehydrothiotoluidin. The mass melts, and the product distills over around 250° C. at 45 m.m. pressure. A small amount of water and thiophenols distills over with it, and the product is therefore crystallized from ethyl alcohol in which it gives an orange-red fluorescent solution. Methyl-thiazlyl-quinolin appears in miscroscopic pale brown crystals melting at 147° C. (cor.). The yield is 2.5 g. or 15% from the equation:

$$C_{14}H_{12}N_2S + C_3H_8O_3 = C_{17}H_{12}N_2S + 4H_2O$$

The product was identical with that obtained in the first experiment, and has a characteristic faint tobacco-like odor.

Qualitative analysis showed the presence of carbon, hydrogen, nitrogen, and sulphur, and the compound was analyzed for sulphur.

Calculated for $C_{17}H_{12}N_2S$	S = 11.59%
Found	S = (11.69% (11.61%

The new base is a typical quinolin and adds methyl iodide directly, a mixture of equal moles of this and quinaldin methiodide reacting in the presence of caustic alkali to produce a substance of a deep purple-red color, analagously to quinolin itself. The product is probably of the cyanine type and it would be interesting to investigate the further condensation of methyl-

benzothiazolyl quinolin methiodide with this, lepidin, other substituted quinolins, as well as with 2-methyl-benzothiazole which Hofmann, as has already been mentioned, observed to undergo similar reactions.

DISCUSSION AND CONCLUSIONS

1. The thiazole structure does not appear to function as a chromophore, or at least, functions very poorly. A large number of benzothiazoles have been described in this paper, and they are representative ones, of which as has been seen, the large majority, even of those which contain groups which are ordinarily accepted as auxochromes, such as the hydroxy, the hydrosulphide, methoxy, ethoxy, nitro (which is also a chromophore), etc., are colorless, and the remainder in a pure state are only faintly colored, as dehydrothiotoluidin, and are not dyes. The primulins and chromins are exceptions but do not furnish a valid objection to this conclusion, as their structure is not yet established. In the dyes of this series, it is therefore concluded, the chromophore must be the azo or other group, though the thiazole structure may, and probably does play an important part in modifying the colors obtained.

2. The thiazole structure is not an odorophore. The odoriferous compounds as may be seen from Hofmann's work and other investigations described herein, are closely related to the mother substance, benzothiazole, and the farther we get from this by substitution, the fainter the odor becomes. In the odorous compounds, as has been previously observed, the smell is strongly suggestive of pyridine and the other nitrogen bases, and appears to be associated with the tertiary nitrogen atom. This is further borne out by another fact developed in this paper. Dehydrothiotoluidin is odorless but the benzothiazolyl quinolin synthesized from it has again the typical plant-base odor somewhat resembling nicotine, which it acquires on the introduction of the second tertiary nitrogen atom. The peculiarly aromatic odor of "Rosenkörper" is hence a purely fortuitous circumstance and indeed, the odor of this when in a pure, dry state is very faint, and it requires some stretch of the imagination to be reminded of "tea-roses and geraniums."

3. The commercial methods by which dehydrothiotoluidin is being prepared at present give yields of the base which do not exceed 35% and some of this must necessarily be lost in subsequent purification. From the work done in this paper, the direct separation of dehydrothiotoluidin and primuline if formed in the same mixture with other substances, does not seem to be possible (other than by distillation) if by such a method is meant one which will give large yields of the base in a state of purity indicated by good crystalline form, and a melting point of 191° or over.

The problem must be solved by the discovery of a method of synthesis which will avoid entirely the simultaneous formation of primulin, if it is to be solved at all.

SUMMARY

1. A fairly complete resume of previous work in the benzothiazole field has been given, the chief contribution of the investigators noted, and some attractive lines for further research have been indicated.

2. The following new compounds have been prepared:

2 Paratolylbenzothiazole
Nitroparatolylbenzothiazole
Aminoparatolylbenzothiazole
22 azo dyes from aminoparatolyl benzothiazole
Tri (2 anilinobenzothiazolyl) carbinol
Di (2 benzothiazolyl) fuchsone benzothiazolylimine
Primulin azo benzolyene urea
Paranitrobenzal paratoluidin
Benzaldehydrothiotoluidin
6 (6 methyl benzothiazolyl) quinolin

3. From the consideration of about one hundred compounds of the benzothiazole group, including those prepared in the course of this work, and others described by previous workers, it has been concluded that the thiazole structure is not a chromophore.

4. Of all the compounds given, only seven have characteristic odors, and only one has one which differs from what we should expect from structural considerations of genetic relationship. It is therefore concluded that the thiazole structure is not an odorphore.

5. Apparatus has been developed and a laboratory method has been given for the preparation of dehydrothiotoluidin in a state of purity, which, judged by its melting point (194.8° C., cor.), has not been attained by previous workers, and a critical study has been made of the reactions and processes by which it is being obtained at present.

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